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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,601	08/11/2006	Hans-Arne Hansson	1033592-000005	6872

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EXAMINER
DUTT, ADITI

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
08/28/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/573,601	HANSSON ET AL.	
	Examiner	Art Unit	
	Aditi Dutt	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-5,16 and 20-43* is/are pending in the application.

4a) Of the above claim(s) *3-5,16,20-22 and 36-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-35,41-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. The amendments to claims and the specification filed on 23 April 2009 have been entered into the record and have been fully considered. Claims 23-24, 26-29, 33, 35 and 41, have been amended. New claim 43 has been added.

2. Claims 23-35, 41-43, drawn to a method of treatment or prevention of a condition associated with a gain or loss of nervous tissue, comprising administering an effective amount of an antisecretory protein or an oligopeptide or derivative, thereof, comprising Formula I, are being considered in the instant application.

Response to Amendment

Withdrawn objections and/or rejections

3. Upon consideration of Applicant's persuasive argument providing the definition of antisecretory factor protein or AF protein as disclosed in the specification, the rejection of claims under 35 U.S.C. 112, second paragraph is withdrawn.

Rejections maintained

35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The rejection of claims 23-35 and 41-42 under 35 U.S.C. 112, first paragraph is applied to the amended claims, and new claim 43 for reasons of record in the Office Action dated 23 December 2008. It is to be noted that the enablement rejection associated with prevention is withdrawn in view of cancellation of the limitation “prevention”. However, the claims recite derivatives of Formula 1.

5. Applicant argues that the SPC induced formation of AF will result in the formation of a full-length AF and other peptides of various lengths due to natural post-translational processing, wherein the full-length peptide, as well as the shorter peptides have biological activity. Citing WO documents (WO 971008202 and WO 2007/126364), Applicant asserts that synthetic peptides produced recombinantly exhibit biological activity similar to the full-length AF protein. Although the documents do not teach the treating of pathological loss of nervous tissue using these peptides, Applicant emphasizes that the skilled person in the art would be motivated to try to rescue neuronal tissue by using the peptides of the invention.

6. Applicant's arguments are fully considered but not found to be persuasive. WO '202 teaches recombinant AF (rAF) activity to inhibit intestinal secretion after cholera toxin challenge using several fragments or derivatives, many of which do not exhibit the activity (Table 1). WO '364 teaches normalization of intraocular hypertension in rodents by administration of AF or AF-16 (amino acids 36-51). However, as also acknowledged by Applicant none of these references teach the administration of derivatives of AF protein to a patient for treating a pathological loss of nervous tissue. As stated in the previous Office Action, it is reiterated as follows:

> It is not even clear from the relevant literature as to what regions of the ASP sequences or the maximum length of the sequences are essential for the claimed biological activity. It also not clear as to what regions of ASP are particularly formed after feeding rats or mice with enriched diet, or as in the instant case with SPC diet. Also unclear is how specific the effect of ASP is, when feeding rats on an enriched diet, especially considering as Kempermann et al. states "factors still unknown, contribute to the enhanced performance induced by exposure to an enriched environment" (page 495, para 1). Thus, undue experimentation would be required of the skilled artisan to identify the precise structural characteristics of the claimed Formula I, or oligos or derivatives thereof having the therapeutic effect in conditions characterized by loss of neuronal cells or tissues.
>
> Additionally, it cannot be concluded with certainty that a "greater number of neurons in the dentate gyrus leads to enhanced behavioral performance" (Kempermann et al., page 495, last para). Since the treatment of a condition in a patient would entail physiological and functional improvement, the instant specification fails to provide adequate guidance to the skilled artisan to make and use the full scope of the inventive method, resulting in undue experimentation to use any oligopeptide or derivative of Formula I for treating the condition in totality.

7. It is further noted that the function cannot be predicted from structure, especially because certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly

involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. The specification's general discussion of making and using derivatives comprising Formula 1 for the claimed therapeutic goal constitutes an invitation to experiment by trial and error. As was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991).

8. Specifically, a proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to generate the infinite number of ASP or Formula I derivatives recited in the claims and possibly screen the same for treatment of conditions associated by CNS tissue loss; the lack of direction/guidance presented in the specification regarding the same; the absence of working examples directed to same; the complex nature of the invention; the state of the prior art establishing that biological activity cannot be predicted based on structural similarity and the unpredictability of the effects of mutation on protein structure and function; and the breadth of the claims which fail to recite any structural or functional limitations and also encompass a broad class of derivatives - undue experimentation would be

required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 USC § 112-Written Description

9. The rejection of claims 23-35 and 41-42 under 35 U.S.C. 112, first paragraph is applied to the amended claims, and new claim 43 for reasons of record in the Office Action dated 23 December 2008.

10. Applicant's arguments are the same as for the 112 first paragraph enablement rejection as summarized above.

11. Applicant's arguments are fully considered but not found to be persuasive for reasons put forth above. As stated in the previous Office Action, it is repeated that the brief description in the specification of one ASP polypeptide (SEQ ID NO: 1), one N-terminal active region comprising Formula I (amino acids 1-163 amino acids of SEQ ID NO: 1), and one ASP oligo (amino acids 35-51 of SEQ ID NO: 1), is not adequate written description of an entire genus of functionally equivalent polypeptides which incorporate all derivatives of ASP or Formula I or SEQ ID NO: 1. With the exception of the ASP polypeptide (SEQ ID NO: 1), one N-terminal active region comprising Formula I (amino acids 1-163 amino acids), and one ASP oligo (amino acids 35-51 of SEQ ID NO: 1), the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation

or production. Therefore, only ASP polypeptide (SEQ ID NO: 1), one N-terminal active region of Formula I (comprising amino acids 1-163 amino acids), one ASP oligo (amino acids 35-51 of SEQ ID NO: 1), but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. The rejection of claims 23-35, and 41-42 under 35 U.S.C. 102(b) as clearly anticipated by St. George-Hyslop et al., (International Application Publication No. WO 97/27296, dated 31 July 1997), as evidenced by Barten et al. (Mol Neurobiol. 37: 171-186, 2008) and Roth et al. (Biol Res 38: 381-387, 2005), is applied to the amended claims, and new claim 43 for reasons of record in the Office Action dated 23 December 2008..

13. Applicant argues that contrary to Examiner's statement that the entire S5A protein is used for treating Alzheimer's Disease (AD), the '296 reference teaches that only a part of S5A corresponding to amino acids 70-377 residues interacts

with presenilin, thereby possibly having an effect on AD. Applicant alleges that the reference does not disclose derivatives comprising an amino acid sequence of Formula 1 that does not encompass 70-377 amino acid residues of S5A, e.g. AF-16 is outside 70-377, thus will not bind to presenilin. Applicant, therefore, asserts that pharmaceutical preparations of only peptides that "include 70-377 of S5A" will be used for treating AD.

14. Applicant's arguments are fully considered but not found to be persuasive. By arguing over the binding regions of S5A to presenilin, Applicant is deriving at conclusions that are not required by the presently claimed inventive method. As stated before, the instant claims recite the administration of AF protein for treatment of loss of nervous tissue, wherein the AF protein or derivatives thereof, comprise Formula 1 or amino acids 1-163 of SEQ ID NO: 1. The reference teaches that the administration of a normal (or full-length) presenilin interacting protein (S5A having homologous sequence comprising 1-163 amino acids as claimed) in pharmaceutical compositions for treatment of diseases like AD (page 74, lines 27-28; page 75, lines 9-20; claim 75), thereby anticipating the claimed invention. Applicant's arguments are directed to mechanistic aspects of presinilin binding domains of S5A, which are not required by the instant claims, rather is irrelevant. Furthermore, the reference does not indicate that pharmaceutical compositions should consist of 70-377 amino acids of S5A, as alleged by Applicant. Because the reference teaches administration of the presenilin binding protein for neurodegenerative disease therapy, wherein the protein encompasses

the full length protein comprising Formula 1 and presenilin binding region, the reference anticipates the invention.

Conclusion

15. No claims are allowed.

16. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

17. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.

19. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on (571) 272-0911. The

fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

20. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov/. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD
14 August 2009

/Jeffrey Stucker/

Supervisory Patent Examiner, Art Unit 1649